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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/108,673	07/01/98	TENG C	ISIS-3105

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EXAMINER	
SANDALS, W	
ART UNIT	**PAPER NUMBER**
1636	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/108,673	Applicant(s) Teng et al
	Examiner WILLIAM SANDALS	Group Art Unit 1636

☒ Responsive to communication(s) filed on *Jul 18, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-40* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-40* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Arguments

1. Applicant's arguments regarding rejections of claims 1-40 filed in Paper No. 12, filed March 30, 2000 have been fully considered but they are not persuasive. All rejections have been sustained and are repeated below along with responses to arguments presented in Paper No. 12.

Double Patenting

2. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

3. Claims 1-24 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-24 of copending Application No. 08/886,829. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 25-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 of copending Application No. 08/886,829. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating, method of investigating of the instant claims 25-40 all require the administration of the claimed pharmaceutical composition to an animal (human), which is a treatment of the animal, making the claimed methods and pharmaceutical compositions patentably indistinct from the claims of the '829 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to pharmaceutical composition, a method of treating and a method of investigating the role of a gene or gene product in an animal having or suspected of having a disease or disorder that is treatable in whole or in part with one or more nucleic acids via the enteral route.

The Specification does not teach one of ordinary skill in the art how to treat or investigate the role of a gene or gene product in an animal (which may be other than a human). Pharmaceutical treatment with nucleic acids is a new and developing art and is highly unpredictable. While the Specification does provide teaching on the introduction of nucleic acids into the blood and generally into the organs of an animal via the enteral pathway which is a step toward a pharmaceutical treatment with nucleic acids, it does not teach one of ordinary skill in the art how to treat nor investigate a role of a gene or gene product with nucleic acids since the practice of the treatment or investigation is highly unpredictable, and would require specific teachings to guide the ordinary skilled artisan how to make and use the claimed invention. As such, specific teachings must be present in the Specification to support any claims to treatment or investigation in an animal with nucleic acid. In order to do so, undue experimentation is

required. Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors as they apply to the instant claimed invention are as follows:

a- The quantity of experimentation necessary to reduce the instant claimed invention to practice would involve delivery via the enteral route of a nucleic acid to an animal and treating the animal with the nucleic acid. Treatment of an animal with a pharmaceutical nucleic acid is a new and developing art, and as such requires detailed teachings on how to make and use such a preparation.

b- The specification teaches the delivery of a nucleic acid via the enteral route to the blood and generally into the internal organs of an animal by cannula delivery of nucleic acids to the small intestine of a rat. There are no teachings of pharmaceutical treatment.

c- The nature of the invention is complex. Treatment of animals with nucleic acids is a new and developing art as taught in Gewirtz et al. (see the entire article). Gewirtz et al. taught the difficulties of therapy with nucleic acids such as antisense oligodeoxynucleotide, stating that there are two major problems which must be overcome. First, the nucleic acid must find its cellular target. Second, it must then find and act on its intracellular target. The specification does not teach one of ordinary skill in the art how to direct the nucleic acid to its cellular target nor how the nucleic acid would then act on its intracellular target.

d- The state of the prior art as taught by Gura (see especially page 575, column 1, second paragraph, and page 576, third paragraph to the end of the article) demonstrates some of the difficulties associated with nucleic acid pharmaceutical therapy, stating "[b]ut the biggest concern is that antisense compounds simply don't work the way researchers once thought they did"...."Besides not always working by 'true antisense mechanisms,' the synthetic oligonucleotides have also caused side effects in experimental animals."

e- The state of the art as recited in Stull et al. (see especially pages 476-478) taught that the stability, affinity, efficiency and subcellular distribution of the nucleic acids in the host animal are all areas of uncertainty and need careful study and analysis before any nucleic acid therapeutic modality can be understood and consistently applied. Also, Agrawal et al. taught the delivery of synthetically modified nucleic acids administered to rats via the oral route. However, the nucleic acids had been specifically modified to resist nuclease digestion. Also, no pharmaceutical therapy was demonstrated by Agrawal et al.

f- The teaching of absorption into the blood and internal organs of the nucleic acids in the instant Specification does not demonstrate any targeting of the nucleic acid to a cell or to intracellular targets as recited by Gewirtz et al., nor does the Specification address any of the issues raised by Gura or Stull et al. Therefore, no pharmaceutical effect has been demonstrated.

g- For the reasons stated by Gewirtz et al., Gura, and Stull et al. the unpredictability of pharmaceutical applications of nucleic acids is very high.

g- Therefore, given the analysis above, it must be considered that the skilled artisan would have needed to have practiced considerable non-routine, trial and error experimentation to enable the full scope of the claims.

Response to Arguments

8. Arguments set forth in Paper No. 10 assert that any utility for the invention which is enabled provides enablement for all claimed applications of the invention. This is not the case, and a pharmaceutical claims which recite nucleic acid must be enabled for pharmaceutical applications of the nucleic acid. As set forth above, the claims are not enabled for a pharmaceutical application of a nucleic acid.

9. Arguments set forth in Paper No. 12 assert that **any utility** (emphasis added) is sufficient to enable the claims to a pharmaceutical composition. As stated above, a pharmaceutical composition has only one utility, namely to treat. The utilities of investigation or studying of a composition do not have a pharmaceutical application. This being the case, the argument is not found convincing.

10. Arguments set forth in Paper No. 12 assert that antisense technology is enabled by the prior art references provided which demonstrate the use of antisense in experimental systems. These references do not provide a nexus to treatment, and as such are not enabling.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 24 recites that the antisense oligonucleotide has "biological activity against" miscellaneous disorders and diseases resulting from infection by HIV or non-retroviral viruses. One of ordinary skill in the art would not know how to identify the "biological activity against" an unspecified disease caused by an unspecified organism. Without proper guidance and instruction from the claims and specification as to the particulars of the "biological activity" or the source of the disease, or the identity of the disease causing organism, the claims are vague and indefinite.

Response to Arguments

14. Arguments set forth in Paper No. 10 assert that the specification taught examples of "biological activity against" for an antisense nucleic acid. Examples are edifying, but fail to provide a definition for the phrase "biological activity against". The specification does not provide clear teaching on the meaning of "biological activity against", as described above, and as such the phrase "biological activity against" is deemed to be vague and indefinite.

15. Arguments set forth in Paper No. 12 assert that a definition of "biological activity against" is provided in the specification at page 33, lines 10-27. The passage cited provides a recitation of some set of undefined genes, or proteins and anything which may act on said genes

or proteins. This set of limitations does not have a clear and well circumscribed meaning. As such the phrase continues to be vague and indefinite.

16. Claim 25 recites a method of treating "a disease or disorder that is treatable in whole or in part with one or more nucleic acids". One of ordinary skill in the art would not know how to identify the "a disease or disorder that is treatable in whole or in part with one or more nucleic acids" since the claim is to an unspecified disease caused by an unspecified cause. Without proper guidance and instruction from the claims and specification as to the particulars of the "disease or disorder that is treatable in whole or in part with one or more nucleic acids", one of skill in the art would not know the metes and bounds of the claim and the claim is vague and indefinite.

Response to Arguments

17. Arguments set forth in Paper No. 10 assert that examples of diseases or disorders which are treatable a taught in the specification. Examples taught in the specification do not provide a definition of the diseases or disorders which are treatable, and do not provide an argument to overcome the rejection as set forth above regarding the teaching to one of ordinary skill in the art as to how to know the metes and bounds of the claims as written.

Conclusion

18. This is an RCE of applicant's earlier Application No. 09/108,673. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.
Examiner
September 15, 2000

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER